

REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, claims 1-3, 13-14 and 51-62 are pending. Claims 4-12 and 15-50 are canceled. Claims 1, 2 and 13 are amended. New claims 51-62 are added.

Claim 1 is amended to set forth that the Pvs25 polypeptide has at least 95% identity to SEQ ID NO:4 and induces an immune response in a susceptible organism that blocks the transmission of malaria. Support is found, for example, on page 7, line 33 through page 8, line 4; on page 8, lines 9-19; and on page 12, lines 27-34 of WO 99/29868.

Claim 2 is amended to become an independent claim, in accordance with the suggestion of the Examiner.

Claim 13 is amended to set forth that the Pvs25 polypeptide has at least 95% identity to SEQ ID NO:4. Support is found, for example, on page 12, lines 27-34.

New claim 51 sets forth an isolated nucleic acid molecule having at least 95% identity to SEQ ID NO:3. Support is found, for example, on page 12, lines 19-22.

New claims 52-53 replace originally filed claims 4-5. Support is found, for example, in originally filed claims 4-5 and on page 12, lines 27-34.

New claims 54-56 replace originally filed claims 6-8. Support is found, for example, in originally filed claims 6-8 and on page 12, lines 27-34.

New claims 57 and 62 set forth routes of administration. Support is found, for example, on page 6, line 26; on page 35, line 16; on page 39, lines 30-32; and on page 40, lines 23-24.

New claims 58-61 replace originally filed claims 9-12. Support is found, for example, in originally filed claims 9-12 and on page 12, lines 27-34.

Request for Rejoinder

Applicants respectfully request rejoinder of the claims in Groups I-III, as defined in the restriction requirement dated October 21, 2005. Applicants respectfully submit that the amended claims are linked by a single general inventive concept under PCT Rules 13.1 and 13.2.

The “special technical feature” of the present invention relates to compositions comprising nucleic acid sequences encoding Pvs25 polypeptides that share at least 95% amino acid sequence identity to SEQ ID NO:4; Pvs25 polypeptides that share at least 95% amino acid sequence identity to SEQ ID NO:4; and nucleic acid sequences encoding Pvs25 polypeptides that share at least 95% nucleic acid sequence identity to SEQ ID NO:3. The Pvs25 nucleic acid sequences and polypeptide sequences of the amended claims clearly are distinguished from the Pfs25 sequences disclosed in WO 89/10936, the only cited art, for the reasons discussed below.

Groups I and II

Groups I and II are related in that the DNAs of Group I encode the polypeptides of Group II. The claims of Group II have been re-presented in amended form as claims 52-56. Example 39 of the PCT International Search and Preliminary Examination Guidelines¹ illustrates the case between the following claims:

Claim 1. Isolated protein X having SEQ ID NO: 1.

Claim 2. Isolated DNA molecule encoding protein X of claim 1.

The Guidelines conclude that “(t)he claimed DNA molecule encodes protein X, and therefore protein X and the DNA encoding protein X share a corresponding technical feature. Consequently, the claims have Unity of Invention.” In view of the above example, Applicants respectfully assert that the Unity of Invention between Groups I and II should be

¹ MPEP Appendix AI, Annex B, “Unity of Invention,” section (1) states that examples giving guidance on how the “unity of invention” principles may be interpreted in particular cases are set out in “the PCT International Search and Preliminary Examination Guidelines” (see, page AI-58 of MPEP, 8th Ed., 2001, Rev. October 2005). Example 39 of the PCT International Search and Preliminary Examination Guidelines is attached as Exhibit A.

acknowledged in the instant case. Accordingly, the Examiner is respectfully requested to withdraw the restriction requirement between the claims of Groups I and II.

Groups II and III

The claims of Groups II and III are related as product and use of the product. The claims of Group III have been re-presented in amended form as claims 58-61. The MPEP follows the PCT International Search and Preliminary Examination Guidelines in stating that PCT Rule 13.2 shall be construed as permitting, in addition to an independent claim for a given product (*e.g.*, a polypeptide), a use of the product (*e.g.* a method of inducing an immune response).² Therefore, Applicants respectfully assert that there is Unity of Invention between Groups II and III, and respectfully request withdrawal of the restriction requirement between these Groups.

Specification

The Examiner objects to the preliminary amendment filed on December 29, 2003 under 35 U.S.C. § 132(a) for allegedly introducing new matter. The Examiner alleges that SEQ ID NOs 16-24 are not in the originally filed specification.

The locations for insertion of amended paragraphs was incorrect in the preliminary amendment filed on December 29, 2003. Amendments made to the specification in the present response delete the incorrectly inserted paragraph and insert the same amended paragraphs into their correct location, corresponding to PCT Publication WO 99/29868.

SEQ ID NOs 16-24 find support in International Application Number PCT/US98/25742, filed on December 4, 1998 (published as WO 99/29868) and U.S. Provisional Patent Application No. 60/067,596, filed on December 5, 1997 as follows:

² See, Section (e)(i) of Annex B of Appendix AI (page AI-59). Page 77 of the PCT International Search and Preliminary Examination Guidelines is included with Exhibit A.

| SEQ ID NO: | WO 99/29868 | 60/067,596 |
|------------|----------------------------------|----------------------|
| 16 | Figure 6 | |
| 17 | Figure 6 | |
| 18 | Figure 6 | |
| 19 | Figure 6 | |
| 20 | page 26, lines 1-4 | page 24, lines 16-19 |
| 21 | page 26, lines 7-10 | page 24, lines 22-25 |
| 22 | page 36, line 21 | page 35, line 9 |
| 23 | page 36, line 21 | page 35, line 10 |
| 24 | page 44, line 2; page 45, line 9 | page 43, line 1 |

In view of the foregoing, the Examiner is respectfully requested to withdraw the objection to the amendment filed on December 29, 2003.

Information Disclosure Statement

The Examiner has requested that the provided references be listed on PTO/SB/08A and 08B forms. In response, Applicants attach to this response PTO/SB/08A and 08B forms listing the references submitted on February 12, 2003.

Claim Objection

The Examiner is thanked for indicating that claim 2 would be allowable if rewritten in independent form. In response, Applicants have rewritten claim 2 in independent form.

Rejection under 35 U.S.C. § 112, first paragraph, written description requirement

The Examiner has rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants do not agree with the Examiner. However, in the interest of furthering prosecution, Applicants have amended claim 1 to set forth an isolated nucleic acid molecule with the structural definition of being at least 95% identical to SEQ ID NO:4, and the functional definition of being a Pvs25 polypeptide that induces an immune response in a susceptible organism that blocks the transmission of malaria. Therefore, amended claim 1 sets forth a nucleic acid that is both structurally and functionally defined. Based on the teachings of the specification, those of skill in the art could recognize that Applicants were in possession of the claimed genus of nucleic acid molecules (*see, for example*, page 7, line 33 through page 8, line 4; page 8, lines 18-21; and page 12, lines 19-27). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 112, first paragraph, enablement requirement

The Examiner has rejected claims 13 and 14 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement.

In order to establish a *prima facie* case of lack of enablement, the Examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ 1510, 1513 (Fed. Cir. 1993). As set forth in MPEP § 2164.01, “the test of enablement is not whether any experimentation is necessary, but whether... it is undue.” Further, the “fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation” (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

The Examiner alleges that the specification does not provide guidance on the induction of any immune response by administering a Pvs25 nucleic acid vaccine by any route. *See*, page 7 of the present Official Action. Applicants respectfully disagree. The present specification teaches that Pvs25 nucleic acids and polypeptides can be administered via several

routes, oral and parenteral, including intramuscular, intradermal, subcutaneous, intranasal, oral, intravenous and topical (*see, for example*, page 6, lines 23-27; page 39, lines 29-32; and page 40, lines 23-24 of WO 99/29868). The specification further teaches that DNA can be injected intramuscularly or intradermally (page 35, line 16). Also, those of skill in the art understood the routes preferred for administration of nucleic acids encoding antigens. *See, for example*, Donnelly (1995) *Ann. NY Acad. Sci.* 772:40 46; Corr (1997) *J. Immunol.* 159:4999 5004; and Manickan (1997) *J. Clin. Invest.* 100:2371 2375, referenced on page 35, lines 17-18. Guides were also available to the skilled person to help determine the preferred route of delivery for a particular purpose. *See, for example*, Grabenstein, *Immunization Delivery: A Complete Guide*, 1997, Facts and Comparisons.

The Examiner also appears to be concerned about the operability of immunizing a susceptible organism with a Pvs25 polypeptide or a nucleic acid encoding a Pvs25 polypeptide of the invention. *See*, page 7 of the present Official Action. Example 5 of the present application shows that recombinant Pvs25 can be used to generate high antibodies titers in mice (page 45, line 30 through page 46, line 23 of WO 99/29868). Example 6 describes an experiment to show that these antibodies prevent oocyst formation in the mosquito gut (page 46, lines 25-34 of WO 99/29868). Applicants subsequently demonstrated, and published in a peer-reviewed manuscript,³ that immunization of mice with Pvs25, as described in the specification, completely prevented oocyst formation in all mosquitoes (*see*, page 6621 of Hisaeda, *et al.*). Applicants used the same test taught in Example 6: test sera was mixed with *P. vivax* gametocytes, fed to mosquitoes, and the number of oocytes in mosquito midguts were counted (*see*, Hisaeda at page 6619). This test is indicative of the *in vivo* efficacy of antisera elicited in a host to block transmission of malaria from a mosquito to a subsequent host.

Applicants have also demonstrated in the present specification that immunizing five different strains of mice (Balb/c, C57BL/6, A/J, B10.BR, CAF1) with Pvs25-containing immunogenic compositions produced high titers of anti-Pvs25 antiserum in all five strains of mice (*see*, page 46, lines 9-20 of WO 99/29868). Those of skill in the art could have a reasonable expectation that anti-Pvs25 antibody titers sufficient to block transmission of malaria

could be successfully generated in higher mammalian hosts without undue expectation. Moreover, successful transmission blocking by immunizing a host with a Pvs25 polypeptide or polynucleotide of the present invention does not necessarily require the immunization of a human host. The present specification demonstrates that mouse anti-Pvs25 antisera completely prevented oocyst formation in mosquitoes. The mosquitoes lacking oocyst formation would be prevented from transmitting malaria to any susceptible host, including humans. Thus, contrary to the Examiner's assertion, the data presented in the present application and in the inventors' subsequent publication demonstrate the *in vivo* efficacy of the claimed invention.

With regard to dosing, Applicants teach that Pvs25 polypeptides or nucleic acids are administered to a patient in an amount sufficient to block transmission of malaria (*see*, page 40, lines 25-28 and page 41, lines 7-12). Those of skill will recognize that the precise amounts administered will depend on several factors (*see*, page 40, lines 29-31 and page 41, lines 10-12). Blocking levels of antibodies in an immunized patient's sera can be measured using techniques well known in the art at the time of the December 1997 priority date of the present application (*e.g.*, ELISA). The ability of a patient's sera to block transmission of malaria can be tested using the assay described on page 46, lines 25-34.

In view of the foregoing, Applicants respectfully submit that the specification teaches those of skill in the art to practice methods without undue experimentation of inducing transmission blocking immune responses in a susceptible organism by administering a therapeutically effective amount of a Pvs25 nucleic acid or polypeptide. The Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected claim 1 under 35 U.S.C. § 102(b) as allegedly anticipated by WO 89/10936 ("Miller"). The Examiner acknowledges that the nucleic acid sequences of Pfs25 and Pvs25 encode proteins with 45% identity (*see*, page 9 of the present Official Action). Applicants do not agree with the Examiner. However, in the interest of furthering prosecution, Applicants have amended claim 1 to set forth a nucleic acid sequence

³ Hisaeda, *et al.*, *Infection and Immunity*, 2000, 68:6618-23 is attached as Exhibit B.

Appl. No. 09/554,960
Amdt. dated April 21, 2006
Reply to Office Action of January 30, 2006

PATENT

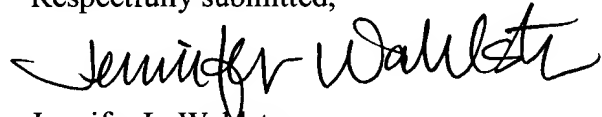
encoding a Pvs25 polypeptide having at least 95% amino acid sequence identity to SEQ ID NO:4. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments
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